

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 September 2000 (04.09.00)	Applicant's or agent's file reference 127,396 PCT
International application No. PCT/IL99/00660	Priority date (day/month/year) 03 December 1998 (03.12.98)
International filing date (day/month/year) 03 December 1999 (03.12.99)	
Applicant SHANI, Arnon et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

27 June 2000 (27.06.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Charlotte ENGER

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

U013484-1

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GOLLER, Gilbert
WOLFF BREGMAN AND GOLLER
P.O. Box 1352
Jerusalem 91013
ISRAEL

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year) 22.02.2001

Applicant's or agent's file reference
127,396 PCT

IMPORTANT NOTIFICATION

International application No.
PCT/IL99/00660

International filing date (day/month/year)
03/12/1999

Priority date (day/month/year)
03/12/1998

Applicant
BEN GURION UNIVERSITY OF THE NEGEV RESEARCH..et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



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Authorized officer

Gallego, A

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 127,396 PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 b. low.	
International application No. PCT/IL 99/ 00660	International filing date (day/month/year) 03/12/1999	(Earliest) Priority Date (day/month/year) 03/12/1998
Applicant BEN GURION UNIVERSITY OF THE NEGEV RESEARCH..et al		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/00660

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01N25/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01N A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 198334 Derwent Publications Ltd., London, GB; Class A97, AN 1983-744808 XP002136272 & JP 58 121212 A (NITTO ELECTRIC IND CO), 19 July 1983 (1983-07-19) abstract	1,2,5, 10-20
X	GB 2 129 302 A (CHEMICAL DISCOVERIES SA) 16 May 1984 (1984-05-16) whole document	1,2,5-7, 10-20
A	US 4 401 456 A (CONNICK JR WILLIAM J) 30 August 1983 (1983-08-30) cited in the application -/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

20 April 2000

Date of mailing of the international search report

04/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Fax: (+31-70) 340-3016

Authorized officer

Decorte, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/00660

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MEINKE L J ET AL: "PHEROMONE DELIVERY SYSTEM: WESTERN CORN ROOTWORM (COLEOPTERA: CHRYSOMELIDAE) PHEROMONE ENCAPSULATION IN A STARCH BORATE MATRIX" JOURNAL OF ECONOMIC ENTOMOLOGY, US, ENTOMOLOGICAL SOCIETY OF AMERICA. COLLEGE PARK, MARYLAND, vol. 82, no. 6, 1 December 1989 (1989-12-01), pages 1830-1835, XP000086080 ISSN: 0022-0493 -----	
A	GB 2 141 932 A (DEXTER CHEMICALS INT LTD) 9 January 1985 (1985-01-09) -----	
A	EP 0 617 051 A (ALLIED COLLOIDS LTD) 28 September 1994 (1994-09-28) -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No



PC 99/00660

Patent document cited in search report	Publication dat	Patent family member(s)	Publication dat
JP 58121212 A	19-07-1983	NONE	
GB 2129302 A	16-05-1984	NONE	
US 4401456 A	30-08-1983	US 4400391 A	23-08-1983
GB 2141932 A	09-01-1985	AU 573591 B	16-06-1988
		AU 2972784 A	03-01-1985
		CA 1250229 A	21-02-1989
		CH 662038 A	15-09-1987
		DE 3422921 A	03-01-1985
		JP 60155105 A	15-08-1985
		ZA 8404591 A	28-08-1985
EP 0617051 A	28-09-1994	AT 121427 T	15-05-1995
		AU 2269488 A	31-03-1989
		DE 3853604 D	24-05-1995
		DE 3853604 T	31-08-1995
		DK 188589 A	20-06-1989
		EP 0305139 A	01-03-1989
		EP 0330692 A	06-09-1989
		ES 2070854 T	16-06-1995
		FI 891918 A	21-04-1989
		WO 8901948 A	09-03-1989
		JP 2500598 T	01-03-1990
		NO 891651 A	20-06-1989

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 127,396 PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IL99/00660	International filing date (day/month/year) 03/12/1999	Priority date (day/month/year) 03/12/1998	
International Patent Classification (IPC) or national classification and IPC A01N25/18			
Applicant BEN GURION UNIVERSITY OF THE NEGEV RESEARCH..et al			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 10 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 27/06/2000		Date of completion of this report 22.02.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Elliott, A Telephone No. +49 89 2399 8218 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IL99/00660

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

4-16	as originally filed		
1,2,2a-2b,3	as received on	14/11/2000 with letter of	10/11/2000

Claims, No.:

8-52	as received on	27/06/2000 with letter of	06/06/2000
1,3-7	as received on	14/11/2000 with letter of	10/11/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☒ the claims, Nos.: 2
- ☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IL99/00660

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,3-52
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1,3-52
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1,3-52
	No:	Claims	-

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IL99/00660

In amended form the application relates to a sustained release dispersion of water insoluble beads, each bead comprising a polymeric matrix comprised of a protein (e.g. gelatin) and a polysaccharide (e.g. an alginate) and containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air. A further independent claim is directed to a process for preparing the dispersion of beads. The beads of the present application are utilised, for example, in crop protection in the form of attractants for insects. In dispersion, the attractants are not released to the atmosphere.

The following documents are referred to in this report:

- D1: DATABASE WPI abstract no. 1983-744808, abstract of JP 58 121212 A (NITTO ELECTRIC IND CO), 19 July 1983
- D2: GB-A-2 129 302 (CHEMICAL DISCOVERIES SA) 16 May 1984
- D3: US-A-4 401 456 (CONNICK JR WILLIAM J) 30 August 1983
- D4: GB-A-2 141 932 (DEXTER CHEMICALS INT LTD) 9 January 1985
- D5: EP-A-0 617 051 (ALLIED COLLOIDS LTD) 28 September 1994
- D6: Journal of Economic Entomology, 82(6), 1 December 1989, pages 1830-1835, Meinke L J et al: 'Pheromone delivery system: western corn rootworm (coleoptera: chrysomelidae) pheromone encapsulation in a starch borate matrix'

V Reasoned statement under Art 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

Novelty (Article 33(2) PCT)

D1 discloses a gel-like body for sustained release of a volatile substance (perfume, repellent, attractant, insecticide, fungicide, etc). The body is comprised of a sodium polyacrylate compound having at least one epoxy group per molecule, cationic surfactant, volatile substance and water. The presently-claimed subject-matter is to be seen as novel over the disclosure of D1 due to the fact that in present claim 1 the polymeric matrix has been restricted to one comprised of a protein and a polysaccharide.

D2 is directed to a method of treating a ground area with a substance. The substance

is applied to the ground area within a body of polymeric material, the substance being dispersed throughout the polymeric material in a state in which it is available for transfer to the environment thereof. The treatment substance is preferably a pheromone and the polymeric material is preferably formed from an acrylamide monomer cross-linked with N,N'-methylene bisacrylamide. The substance being dispersed is to either act as a repellent or attractant. Insecticides, fungicides, nematocides, acaricides, bactericides or growth hormones may also be employed. The substance is absorbed into the polymer in a liquid medium (water). A detergent, e.g. Triton X-100, is also incorporated. The subject-matter of the present application is to be seen as novel with respect to D2 due to the restrictions made to claim 1.

D3, which the applicant has cited as background art, discloses a method for preparing alginate gel beads containing bioactive materials dispersed therein. The method of preparation comprises mixing alginate for gelation with bioactive material (cf. column 4, lines 12-18 for D3's definition of bioactive materials) in water, preparing a water-soluble metal salt (e.g. CaCl_2 , BaCl_2 or CuCl_2) aqueous solution, dropping the alginate/bioactive material solution into the salt solution whereby alginate gel beads containing the bioactive material are formed. The beads are then separated from the solution. Surfactants and gums are mentioned as optional ingredients (cf. column 5, lines 48-55 & column 6, lines 3&4). Example 11 prepares beads based on sodium alginate and xanthan gum (a polysaccharide) with 2,4-D being the bioactive material (non-volatile). Novelty can be acknowledged with respect to D3 as D3 does not disclose a dispersion of beads having the composition as presently-claimed.

D4 discloses pest control compositions based on a pheromone (inhibitor) in a liquid or semi-liquid polymeric water-resistant matrix allowing sustained release of the pheromone (inhibitor). The polymer matrix is a copolymer of a hydrophobic and a hydrophilic monomer, especially a polymer or copolymer resulting from the polymerisation of monomers selected from vinyl pyrrolidone, esters of acrylic or methacrylic acid, vinyl acetate and styrene. The compositions are applied by spraying to provide spots of the composition containing 2-10 mg of the active material. The compositions of D4 contain neither water nor surfactant and are not based upon a polymeric matrix made up of a protein and polysaccharide. Novelty is acknowledged with respect to D4.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IL99/00660

D5 discloses polymeric compositions for the controlled release of a perfume, more specifically an agricultural semiochemical, e.g. an insect repellent or attractant (cf. D5, page 3, lines 36-51). The polymeric compositions are made up of the active ingredient releasably contained within polymer particles. The particles are emulsion polymerised particles of size $< 1 \mu\text{m}$ (90% by wt.). The compositions are oil-in-water emulsions of the polymer particles formed by the o-i-w emulsion polymerisation of water insoluble monomeric material in which the active ingredient is dissolved; at least 60 wt. % of the monomeric material is selected from one or more alkyl (meth)acrylates and blends thereof with one or more styrenes. On page 5, lines 36&37 it is stated that "conventional surfactant or surfactant blends may be used to facilitate the formation of the emulsion and to stabilise it". Presently-claimed subject-matter is novel over D5 due to the difference in the polymeric matrix used.

D6 discloses a pheromone delivery system. The sex pheromone of the western corn rootworm, *diabrotica virgifera virgifera* LeConte, racemic 8-methyl-2-decyl-propanoate (MDP) is encapsulated in a starch borate (SB) matrix to create a controlled release granular formulation. The formulation of D6 is to be seen as completely different to that presently-claimed; novelty is acknowledged with respect to D6.

Inventive Step (Article 33(3) PCT)

Document D3 is to be seen as the closest prior art to the present application as it discloses beads having a similar composition to the beads in the present dispersion (cf. Example 11 of D3). D3 also states that insect pheromones are to be included under the list of bioactive materials which can be incorporated into the beads of D3.

The object of the present application is to be seen as the provision of a delivery system for volatile bioactive substances, e.g. pheromones.

Although the beads themselves may be made obvious by the disclosure of D3, a dispersion of the water insoluble beads is not contemplated by D3 as a way of storing the beads so that the active material is not released until the beads are actually used. The objective of the present application has therefore been met in a non-obvious manner. The subject-matter of claims 1,3-52 presently on file is therefore seen to be

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IL99/00660

the result of an inventive step (Article 33(3) PCT).

VII Certain defects in the international application

- i. The unit of density lbs/ft³ has been used on page 5 of the application. This should be replaced by the corresponding density in SI units, the original expression being however retained in parentheses.
- ii. There is no claim 2.

VIII Certain observations on the international application

Claim 16 mentions that the attractant can be a "leaf alcohol". It is unclear what the applicant means by a "leaf alcohol".

531 Rec'd PC 856795
24 MAY 2001

1

SUSTAINED RELEASE POLYMER-BASED WATER INSOLUBLE BEADS

The present invention relates to a sustained release dispersion of water insoluble beads and to a process for the preparation thereof. More particularly, the present invention relates to a sustained release dispersion of water insoluble beads each bead comprising a polymeric matrix comprised of a protein and a polysaccharide and containing at least one volatile hydrophobic component for release therefrom in atmospheric air.

U.S. Patents 4,400,391 and 4,401,456 describe and claim alginate gel beads containing bioactive materials dispersed therein. These beads can be made to either float or sink in aqueous environments, and are capable of providing the controlled release of their bioactive materials when applied to terrestrial or aqueous environments.

The prior art deals with the controlled and/or sustained release of various materials from polysaccharide beads such as from alginate gel beads into aqueous or wet environments, however the release of hydrophobic volatile materials into the atmosphere from such a bead is neither taught nor suggested in the prior art.

With this state of the art in mind, there is now provided according to the present invention a sustained release dispersion of water insoluble beads, each bead comprising a polymeric matrix comprised of a protein and a polysaccharide and containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.

In especially preferred embodiments of the present invention, said polysaccharide is selected from the group consisting of sodium alginate, carraggenan, guar gum, locus bean gum, chitosan, pectin carboxy methyl cellulose.

AMENDED SHEET

In other preferred embodiments of the present invention, said protein is selected from the group consisting of gelatin, albumin, casein and Lactoglobulin.

In preferred embodiments of the present invention said surface active molecule is selected from the group consisting of a protein, a monomeric surfactant and a polymeric surfactant.

In especially preferred embodiments of the present invention, said surface active molecule is selected from the group consisting of ethoxylated sorbitan ester, alkyl ether, a block copolymer and gelatin.

Preferably, said bead is of a size between 0.5 micron and 1 mm and especially preferred are beads of a size between 5 and 80 microns.

In preferred embodiments of the present invention said volatile component is an attractant which is preferably selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.

In other preferred embodiments of the present invention said volatile component is an attractant inhibitor which is preferably selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.

In another aspect of the present invention there is now provided a process for preparing sustained-release polymer-based water insoluble beads for release of a volatile hydrophobic component therefrom in atmospheric air, comprising:

- a) preparing an oil/water emulsion by homogenizing a volatile hydrophobic component in water, using at least one surface active molecule;
- b) mixing said emulsion with at least one water-soluble polymer and optionally rehomogenizing the mixture; and
- c) adding the emulsion prepared in step (b) in a dropwise manner into a gellant solution to form said water insoluble beads.

2a

In preferred embodiments of the present invention said process further comprises the step of chemically cross-linking polymers present in said composition and further comprises the step of drying said beads.

The beads prepared by the process of this invention are useful in providing sustained release of volatile materials contained therein, when exposed to the atmosphere. As long as the dispersion of beads are kept in water, the volatile material is not released.

Said oil in water emulsion is preferably prepared by homogenization of the volatile hydrophobic component in a gelatin solution. A water-soluble salt of alginic acid is mixed with water and added to the solution. The mixture is then homogenized again, and added dropwise into an aqueous solution of di-, tri- or quatra-valent metal salt (called the gellant solution) that will cause the alginate to form gel. As each drop comes in contact with the metal salt solution, the gelation is initiated and a bead forms. Further treatment of the water insoluble beads with tannic acid solution over night is possible if an extended delay of the release of the volatile material is desired.

More particularly, the invention describes the process and the product, which is the formulation for a slow release of pheromones.

The abstract of JP 58 121212 (D1) discloses a gel like body for sustained release of a volatile substance. The polymer is comprised of sodium polyacrylate having at least one epoxy group per molecule and a cationic surfactant. The resulting gel like body which is composed of synthetic polymers is different from the polymeric beads of the present invention, which are based on biopolymers, proteins and polysaccharide. The use of biopolymers has significant advantages based on environmental considerations.

2b

GB 2, 129,302 (D2) describes a method of treating a ground area with a substance which is dispersed within a polymeric material. The method of preparation of the product described therein is completely different from that of the present invention and is based on polymerization of synthetic monomers, which forms a large body of polymeric material, which has to be sliced or diced or otherwise divided into small particles. In contradistinction the present invention deals only with biopolymers and the cross-linking of polymers which were already formed by multivalent electrolytes leading to small particles. In addition, since this method is based on chemical reaction, the monomers may react with the active substance.

US Patent 4,401,456 (D3) describes a method for preparing alginate beads containing bioactive material, which mainly is released by leaching. The beads do not contain, as in the present invention, a protein, in addition to the alginate and said patent suggests only the use of alginate and not the use of other polysaccharides.

GB 2,141,932 (D4) discloses pest control composition based on a pheromone in a liquid or semi-liquid polymeric water resistant matrix allowing sustained release of the pheromone. Unlike the present invention, the composition is not based on beads, does not contain water and surfactant, and is based on synthetic polymers.

EP 0 617 051 describes polymeric compositions for controlled release of substances, in the form of emulsions which are used for impregnation or coating articles. In said Patent, unlike the present invention, the polymers are synthetic and the active substance is in direct contact with the monomers and therefore may react with the monomers and lose its activity.

In Journal of Economic Entomology, 82(6), 1 December 1989, pages 1830-1835, Meinke L J et al: describes a pheromone delivery system which is encapsulated in a starch borate matrix. The formulation is completely different than the compositions described in the present invention.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

In substantial similarity to U.S. 4,401, 456, the simplicity of requirements needed for carrying out the process of the present invention permits much latitude in design of equipment. A suitable apparatus, as described below, is brought only for the purpose of illustration and not to be construed as limiting the invention. The apparatus consists of a reservoir to contain the alginate/protein/volatile- material/water emulsion that is equipped with a stopcock or similar device that allows the dropwise addition of the mixture through an orifice. The gellant solution may be contained in any convenient vessel.

After a suitable amount of time within the gellant solution, the resulting gel beads are removed by means such as filtration, screening, or straining. They may be rinsed in plain water if desired.

Beads may be further stirred in tannic acid solution and then rinsed again if a longer release-time of the volatile material is desired

The beads can be used in this fully hydrated state or dried to any desired moisture content without losing their effectiveness. Small hard granules result when the beads are dried. The hydrophobic oil which is present within the beads, e.g. a pheromone, can be released slowly, to the atmosphere. The rate of release can be sustained by suitable selection of the concentration of the alginate, proteins, tannic acid and additional components such as polyethylene glycol, urea and electrolytes.

WHAT IS CLAIMED IS:

1. A sustained release dispersion of water insoluble beads, each bead comprising a polymeric matrix comprised of a protein and a polysaccharide and containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.
3. A sustained release dispersion of water insoluble beads according to claim 1, wherein said protein is selected from the group consisting of gelatin, albumin, casein and Lactoglobulin.
4. A sustained release dispersion of water insoluble beads according to claim 1, wherein said polysaccharide is selected from the group consisting of sodium alginate, carraggenan, guar gum, locus bean gum, chitosan, pectin carboxy methyl cellulose.
5. A sustained release dispersion of water insoluble beads according to claim 1, wherein said surface active molecule is selected from the group consisting of a protein, a monomeric surfactant and a polymeric surfactant.
6. A sustained release dispersion of water insoluble beads according to claim 1, wherein said surface active molecule is selected from the group consisting of ethoxylated sorbitan ester, alkyl ether, a block copolymer and gelatin.
7. A sustained release dispersion of water insoluble beads according to claim 1, wherein each of said beads is of a size between 0.5 micron and 1 mm.

8. A sustained release dispersion of water insoluble beads according to claim 1, wherein each of said beads is of a size between 5 and 80 microns.
9. A sustained-release polysaccharide-protein water insoluble beads according to claim 1, comprising an emulsion of at least one protein and at least one volatile hydrophobic component contained therein, wherein said volatile component is released from said water insoluble bead in atmospheric air.
10. A sustained-release dispersion of water insoluble beads according to claim 1, wherein said volatile component is a bioactive material.
11. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is a pheromone.
12. A sustained-release dispersion of bead according to claim 11, wherein said pheromone is selected from the group consisting of grandlure, muscalure, gosiplure and disparlure.
13. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is an essential oil.
14. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is a pesticide.
15. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is an attractant.
16. A sustained-release dispersion of bead according to claim 15, wherein said attractant is selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.
17. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is an attractant inhibitor.
18. A sustained-release dispersion of bead according to claim 17, wherein said attractant inhibitor is selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.

19. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is present in an amount of up to 50% wt./wt.
20. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is present in an amount of up to 20% wt./wt.
21. A sustained-release dispersion of bead according to claim 1, wherein said protein is a gelatin.
22. A sustained-release dispersion of bead according to claim 21, wherein said gelatin is a type B gelatin.
23. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is Eugenol.
24. A sustained-release dispersion of bead according to claim 1, further comprising tannic acid for effecting a slower release rate.
25. A process for preparing a sustained-release dispersion of water insoluble beads for release of a volatile hydrophobic component therefrom in atmospheric air, comprising:
 - a) preparing an oil/water emulsion by homogenizing a volatile hydrophobic component in water, using at least one surface active molecule;
 - b) mixing said emulsion with at least one water-soluble polymer and optionally rehomogenizing the mixture; and
 - c) adding the emulsion prepared in step (b) in a dropwise manner into a gellant solution to form said water insoluble beads.
26. A process according to claim 25, further comprising the step of chemically cross-linking polymers present in said composition.
27. A process according to claim 25, further comprising the step of drying said beads.
28. A process according to claim 25, wherein said gellant solution is selected from the group consisting of an electrolyte solution, a multivalent ion solution, a lower pH solution and a high pH solution.

29. A process according to claim 25, wherein said volatile component is a bioactive material.
30. A process according to claim 25, wherein said volatile component is A pheromone.
31. A process according to claim 30, wherein said pheromone is selected from the group consisting of grandlure, muscalure, gosiplure and disparlure.
32. A process according to claim 25, wherein said volatile component is an essential oil.
33. A process according to claim 25, wherein said volatile component is a pesticide.
34. A process according to claim 25, wherein said volatile component is an attractant.
35. A process according to claim 34, wherein said attractant is selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.
36. A process according to claim 25, wherein said volatile component is an attractant inhibitor.
37. A process according to claim 36, wherein said attractant inhibitor is selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.
38. A process according to claim 25, wherein said volatile component is present in an amount of up to 50% wt./wt.
39. A process according to claim 25, wherein said volatile component is present in an amount of up to 20% wt./wt.
40. A process according to claim 25, wherein said surface active molecule is a gelatin.
41. A process according to claim 40, wherein said gelatin is a type B gelatin.
42. A process according to claim 25, wherein said gellant is an aqueous metal salt solution.

43. A process according to claim 42, wherein said aqueous metal salt solution comprises a divalent or trivalent metal salt.
44. A process according to claim 42, wherein said metal salt solution comprises chlorides and acetates of calcium, barium and copper.
45. A process according to claim 25, wherein the emulsion of step (b) is sprayed into said gellant to form micron-sized beads.
46. A process according to claim 25, wherein said polymer is a polysaccharide.
47. A process according to claim 46, wherein said polysaccharide is alginate.
48. A process according to claim 47, wherein said alginate is a water-soluble salt of alginic acid.
49. A process according to claim 47, wherein said alginate is a water-soluble salt of organic bases.
50. A process according to claim 47, wherein said alginate is selected from the group consisting of sodium, potassium, magnesium, ammonium alginate and amines.
51. A process according to claim 47, wherein said alginate is present in an amount of about between 0.1 and 5% wt./wt.
52. A process according to claim 47, wherein said alginate is present in an amount of about between 1 and 1.5% wt./wt.

AMENDED SHEET

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(54) Title: SUSTAINED RELEASE POLYMER-BASED WATER INSOLUBLE BEADS (57) Abstract <p>The invention provides a sustained release, polymer-based, water insoluble bead, comprising a polymeric matrix containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.</p>		

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SUSTAINED RELEASE POLYMER-BASED WATER INSOLUBLE BEADS

The present invention relates to a sustained release polymer-based water insoluble bead and to a process for the preparation thereof. More particularly, the present invention relates to a sustained release polymer-based water insoluble bead containing at least one volatile hydrophobic component for release therefrom in atmospheric air.

U.S. Patents 4,400,391 and 4,401,456 describe and claim alginate gel beads containing bioactive materials dispersed therein. These beads can be made to either float or sink in aqueous environments, and are capable of providing the controlled release of their bioactive materials when applied to terrestrial or aqueous environments.

The prior art deals with the controlled and/or sustained release of various materials from polysaccharide beads such as from alginate gel beads into aqueous or wet environments, however the release of hydrophobic volatile materials into the atmosphere from such a bead is neither taught nor suggested in the prior art.

With this state of the art in mind, there is now provided according to the present invention a sustained release, polymer-based, water insoluble bead, comprising a polymeric matrix containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.

In preferred embodiments of the present invention said polymeric matrix comprises at least one polymer selected from the group consisting of a protein, a polysaccharide and a synthetic polymer.

In especially preferred embodiments of the present invention, said polysaccharide is selected from the group consisting of sodium alginate, carraggenan, guar gum, chitin, locus bean gum, chitosan, pectin carboxy methyl cellulose.

In other preferred embodiments of the present invention, said protein is selected from the group consisting of gelatin, albumin, casein and Lactoglobulin.

In preferred embodiments of the present invention said surface active molecule is selected from the group consisting of a protein, a monomeric surfactant and a polymeric surfactant.

In especially preferred embodiments of the present invention, said surface active molecule is selected from the group consisting of ethoxylated sorbitan ester, alkyl ether, a block copolymer and gelatin.

Preferred surface active molecules are selected from the group consisting of Tween 80 ®, Tween 20 ®, Span 80 ®, Pluronic F 68 ® and Sodium dodecyl Sulphate.

Preferably, said bead is of a size between 0.5 micron and 1 mm and especially preferred are beads of a size between 5 and 80 microns.

Said beads may be sprayed by conventional sprayers used in agriculture.

Said beads in micron size are preferably kept as dispersions in aqueous solutions, which dispersions may optionally include formulation aids such as sticking agents, wetting agents, uv stabilizers, viscosity-modifying agents and humectants.

In preferred embodiments of the present invention said volatile component is an attractant which is preferably selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.

In other preferred embodiments of the present invention said volatile component is an attractant inhibitor which is preferably selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.

In another aspect of the present invention there is now provided A process for preparing sustained-release polymer-based water insoluble beads for release of a volatile hydrophobic component therefrom in atmospheric air, comprising:

- a) preparing an oil/water emulsion by homogenizing a volatile hydrophobic component in water, using at least one surface active molecule;
- b) mixing said emulsion with at least one water-soluble polymer and optionally rehomogenizing the mixture; and
- c) adding the emulsion prepared in step (b) in a dropwise manner into a gellant solution to form said water insoluble beads.

In preferred embodiments of the present invention said process further comprises the step of chemically cross-linking polymers present in said composition and further comprises the step of drying said beads.

The beads prepared by the process of this invention are useful in providing sustained release of volatile materials contained therein, when exposed to the atmosphere. As long as the beads are kept in water, the volatile material is not

released.

Said oil in water emulsion is preferably prepared by homogenization of the volatile hydrophobic component in a gelatin solution. A water-soluble salt of alginic acid is mixed with water and added to the solution. The mixture is then homogenized again, and added dropwise into an aqueous solution of di-, tri- or quatra-valent metal salt (called the gellant solution) that will cause the alginate to form gel. As each drop comes in contact with the metal salt solution, the gelation is initiated and a bead forms. Further treatment of the water insoluble beads with tannic acid solution over night is possible if an extended delay of the release of the volatile material is desired.

More particularly, the invention describes the process and the product, which is the formulation for a slow release of pheromones.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

In substantial similarity to U.S. 4,401, 456, the simplicity of requirements needed for carrying out the process of the present invention permits much latitude in design of equipment. A suitable apparatus, as described below, is brought only for the purpose of illustration and not to be construed as limiting the invention. The apparatus consists of a reservoir to contain the alginate/protein/volatile-material/water emulsion that is equipped with a stopcock or similar device that allows the dropwise addition of the mixture through an orifice. The gellant solution may be contained in any convenient vessel.

After a suitable amount of time within the gellant solution, the resulting gel beads are removed by means such as filtration, screening, or straining. They may be rinsed in plain water if desired.

Beads may be further stirred in tannic acid solution and then rinsed again if a longer release-time of the volatile material is desired

The beads can be used in this fully hydrated state or dried to any desired moisture content without losing their effectiveness. Small hard granules result when the beads are dried. The hydrophobic oil which is present within the beads, e.g. a pheromone, can be released slowly, to the atmosphere. The rate of release can be sustained by suitable selection of the concentration of the alginate, proteins, tannic acid and additional components such as polyethylene glycol, urea and electrolytes.

The rate of addition of the mixture from the reservoir is a function of orifice size and the number of orifices used. The above rate can be increased by applying air or piston pressure.

The distance between the orifice and the surface of the gellant solution should be far enough to allow the droplet to penetrate the surface of the gellant solution.

The size of the resulting alginate gel beads depends on the viscosity of the alginate/volatile material/water mixture, the amount of water retained in the beads, and orifice size. An orifice of 0.1-5 mm in diameter is suitable, but the preferred range is 0.8-2 mm. Beads will be generally spherical or ellipsoidal with an average diameter of 0.1-6 mm. Smaller beads, down to micron in size, may be prepared by spraying the alginate/volatile material/water mixture into the gellant bath.

A continuous process of producing beads is possible and requires continuous removal of gel beads and maintenance of the gellant concentration. It is also possible to extrude the alginate/volatile- material/ water mixture into the gellant to form a string-like gel, which can be cut into various lengths or dried and ground into granules.

Hydrated (undried) beads will usually be stored in water. The well-known phenomenon of syneresis can occur with alginate gels as well as with many other polysaccharide gels. Specifically, it is the loss of fluid (mostly water in the present invention), from the gel caused by contraction. Most of the fluid loss occurs within the 24-hour period after preparation, but it can continue for a few weeks before coming to equilibrium. Some factors that influence the amount of syneresis are alginate composition, cross-linking of the gelatin with tannic acid, temperature, gellant and the chemical nature of the volatile material. Usually the fluid that is exuded during the first 36 hours, is principally water and only a relatively small amount of volatile material is lost.

The protein used in the emulsion preparation of the present invention is a B type gelatin, but other proteins may be used as well. The concentration of the protein may vary widely and will influence the release rate of the volatile component/s.

The alginates used in the invention are any water-soluble salts of alginic acid. These include sodium, potassium, magnesium and ammonium alginate, and

the alginates of organic bases such as amines. Sodium alginate is preferred. The viscosity of the alginate may vary and will influence gel strength to some degree. Highly refined alginates are not required for the practice of this invention.

An especially preferred alginate is the alginic acid, sodium salt, LX0450, available from MCB Manufacturing Chemists Inc., Cincinnati, Ohio, having a bulk density of 43 lbs./cu ft, a pH of 7.2 in a 1% aqueous solution, and a viscosity (run with a Brookfield LVF @ 60 RPM) of 400 @ 1% and 3500 @ 2%.

Concentration of the alginate formulated in the initial alginate/volatile material/water mixture is 0.1-3% by weight, but 1-1.5% is usually preferred. The volatile materials referred to in this invention are any volatile bioactive materials, such as pheromones, essential oils, pesticides, fragrances, etc.

The excellent chemical compatibility of alginates allows admixture according to the present invention with a very wide choice of volatile materials such as those described above. They are too numerous to list in their entirety. The following are only a few of the pheromones that can be used, given for the purpose of illustration and should not be construed as limiting the scope of the invention. The common name is given first, followed by the chemical name.

Common name**Chemical name**

Muscamone	(Z)-9-tricosene
Gossypure	(ZZ)-7,11-hexadecadien-1-ol acetate, and (Z,E)-7,11-hexadecadien-1-ol acetate
Disparlure	cis-7,8-epoxy-2-methyloctadecane
Grandlure	(1R-cis)-1-methyl-2-(1-methylethenyl cyclobutaneethanol; (Z)-2-(3,3-dimethylcyclohexylidene)ethanol (Z)-(3,3-dimethylcyclohexylidene) acetaldehyde; and (E)-(3,3-dimethylcyclohexylidene) acetaldehyde

It is an important part of this invention that additional control over rate of release of these types of volatile materials may be achieved. This may be achieved by interaction between the components of the formulation with the active materials.

Concentration of the volatile material formulated in the alginate/protein/volatile material/water mixture can be as high as 50% by weight, but is preferably in the range of 0.1-20%. The ingredients of this mixture may be incorporated in any order desired prior to the emulsification process. The preferred pH range of the mixture is 4-12. The usual and preferred temperature of the mixture is 20-30°C, but may be higher to reduce viscosity.

Cations that will gel alginate solutions are the cations of barium, lead, copper, iron, strontium, cadmium, calcium, zinc, nickel, aluminum, tin, acid (H^+), and mixtures of these. The gellant solution of the present invention consists of an aqueous solution of a soluble and ionized salt of a metal listed above, an acid, or a mixture of these. Choice of gellant will have an effect on gel properties and possibly on the release rate of the volatile material dispersed in the alginate gel bead. The preferred gellants are the chlorides and acetates of calcium, barium and copper; the preferred acids are hydrochloric and acetic. Concentration of the metal salt or acid in the gellant solution may be up to 50% by weight, though 1-15% is preferred. Gelation proceeds faster as the concentration is increased. Reaction with sodium alginate and certain volatile materials will reduce the effective concentration of gellant cations, therefore a sufficient concentration must be maintained to provide the desired properties.

Temperature of the gellant solution can affect gel properties. It is an advantage of the present invention, which involve volatile materials that heat does not have to be employed and most products can be made at 1-30°C. The preferred range is 20-30°C. However, any temperature up to, and including, the boiling point of the gellant solution may be used. Reaction of the alginate/volatile material/water mixture with the gellant solution is very rapid and produces a distinct gel bead immediately. Gelation proceeds from the outer surface to the center of the bead. Final gel properties such as hardness, pore size, surface area, strength, elasticity, size, durability, and release rate of the volatile material are influenced by the time within the gellant solution and should be optimized for each product. Generally, a residence time of 0.1-25 minutes may be used, but 1-10 minutes is usually sufficient.

In certain applications it may be desirable to add other ingredients to the alginate/volatile material/water mixture or to the gellant solution, or to the final gel beads. These additives may serve to alter the rate of release of the volatile material, protect the gel beads from microbial attack or oxidation, facilitate the preparation process or reduce syneresis. They include solubilizing agents, biocides such as formaldehyde, enzymes, organic solvents, surfactants, viscosity modifiers, filmforming agents, natural and synthetic gums, sequestering agents, starch, talc, fibers, light-screening chemicals and antioxidants.

Sustained release refers to formulations or materials that dispense their active ingredients into the environment over a period of time in a constant rate. For the purpose of this invention this time period can be short and measured in minutes or hours, or long and measured in days or even months. In the present invention, release of the volatile material from the alginate beads occurs through processes such as leaching, diffusion, dissolution, and degradation in atmospheric air.

Sustained release materials may be used to reduce the number of applications needed to perform a certain task, permit an effective (while not too high) concentration in the environment at any one time, and enhance effectiveness against the target species.

This invention is suitable for producing alginate gel beads containing volatile material, said beads being useful for agricultural, industrial, domestic and health-related purposes.

While the invention will now be described in connection with certain preferred embodiments in the following examples so that aspects thereof may be more fully understood and appreciated, it is not intended to limit the invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalents as may be included within the scope of the invention as defined by the appended claims. Thus, the following examples which include preferred embodiments will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purposes of illustrative discussion of preferred embodiments of the present invention only and are presented in the cause of providing what is believed to be the most useful and readily understood description of formulation procedures as well as of the principles and conceptual aspects of the invention.

EXAMPLE 1

3 grams of gelatin_type B were dissolved in 97 grams of water. 5 grams of dodecyl acetate and 3.4 grams of water were added to 16.6 grams of the solution, and the mixture was homogenized for 5 minutes (9500 R.P.M). 2 grams of sodium alginate were dissolved in 98 grams of water, and 25 grams of the solution were added to the solution of gelatin and dodecyl acetate. The whole mixture was homogenized for 5 minutes (9500 R.P.M).

The solution was added dropwise through a syringe equipped with a 22G x 1 ½ needle, falling a distance of 60 mm, into 150 ml of 1% CaCl₂ solution. The CaCl₂ solution was contained in a 150 mm diameter vessel, and stirred with a magnetic stirrer in a rate of about 120 R.P.M. The rate of addition was such that 5 minutes were required for the 50g addition to take place. The beads formed (2 mm diameter) were left in the solution for 5 additional minutes. The beads were then separated by filtration through a sieve, washed in water and stored in water. When air-dried, the beads became hard granules of about 1 mm in diameter.

Release rate was measured – see sample A in Table 1.

EXAMPLE 2

Beads were made in the same manner as in example 1, using CaCl₂ 0.25% as the gellant solution.

Release rate was measured – see sample B in Table 1.

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EXAMPLE 3

Beads were made in the same manner as in example 1, using CaCl_2 0.1% as the gellant solution.

Release rate was measured – see sample C in Table 1.

EXAMPLE 4

Beads were made in the same manner as in example 1, with 1% gelatin as the protein.

Release rate was measured – see sample D in Table 1.

EXAMPLE 5

Beads were made in the same manner as in example 1, with 0.5% gelatin as the protein.

Release rate was measured – see sample E in Table 1.

EXAMPLE 6

Beads were made in the same manner as in example 1, with 0.6% alginate.

Release rate was measured – see sample F in Table 1.

EXAMPLE 7

Alginate beads containing dodecyl acetate were prepared as in example 1, but using FeCl_3 as the gellant solution.

EXAMPLE 8

Alginate beads containing dodecyl acetate were prepared as in example 1, but using SnCl_4 as the gellant solution.

EXAMPLE 9

Alginate beads containing dodecyl acetate were prepared as in example 1, but the beads formed were left over night in a 1% tannic acid solution. The beads were then washed in water and stored in water.

Release rate was measured – see sample G in Table 1.

EXAMPLE 10

3 grams of gelatin were dissolved in 97 grams of water. 5 grams of Gossypure (Pink Bollworm pheromone) and 3.4 grams of water were added to 16.6 grams of the solution, and the mixture was homogenized for 5 minutes (9500 R.P.M). 2 grams of sodium alginate were dissolved in 98 grams of water, and 12.5 grams of the solution were added to the solution of gelatin and Gossypure. The whole mixture was homogenized for 5 minutes (9500 R.P.M). The resulting

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emulsion was processed as in example 1 to produce alginate gel beads containing Gossyplure.

Release rate was measured – see sample H in Table 1 and Figure 1.

EXAMPLE 11

3 grams of gelatin were dissolved in 97 grams of water. 5 grams of Eugenol and 3.3 grams of water were added to 16.6 grams of the solution, and the mixture was homogenized for 5 minutes (9500 R.P.M). 3 grams of sodium alginate were dissolved in 97 grams of water, and 25 grams of the solution were added to the solution of gelatin and Eugenol. The whole mixture was homogenized for 5 minutes (9500 R.P.M).

The solution was added dropwise through a syringe equipped with a 18G x 1 ½ needle, falling a distance of 500 mm, into 150 ml of 0.25% CaCl₂ solution. The CaCl₂ solution was contained in a 150 mm diameter vessel, and stirred with a magnetic stirrer in a rate of about 120 R.P.M. The rate of addition was such that 5 minutes were required for the 50g addition to take place. The beads formed (2 mm in diameter) were left in the solution for 5 additional minutes. The beads were then separated by filtration through a sieve, washed in water and left overnight in a 1% tannic acid solution. The beads were then washed and stored in water. When air-dried, the beads became hard granules of about 0.5 mm in diameter.

Release rate was measured – see sample I in Table 1.

EXAMPLE 12

Beads were made from an emulsion of 10% Eugenol, 1% gelatin and 1.5% alginate, in the same manner described above. The beads were placed in traps that were placed in a peanut- field. Together with these traps, reference traps that contained live virgin females of the beetle *Maladera Matrida Argaman* were placed in the field. After ten days, the traps containing the eugenol beads trapped as many beetles as the traps with the live females.

EXAMPLE 13

Beads were made from an emulsion of 10% pheromone of the *Pink Bollworm* moth, 1% gelatin and 1% alginate, in the same manner described above. The beads were placed in bags, containing 200 mg of dry beads each. 25 bags were placed in a cotton field, forming a square of 50X50 meters. Reference traps containing pheromone impregnated in cardboard were placed in the middle of the

square and in the field, away from the experiment. In a 43 day period, the reference traps in the field around the experiment trapped much more moths than the trap in the middle of the square as described in Table 2 hereinafter:

EXAMPLE 14

3 grams of gelatin Type B 75 Bloom were dissolved in 97 grams of water. 5 grams of pink bollworm pheromone and 3.4 grams of water were added to 16.6 grams of the solution, and the mixture was homogenized for 5 minutes (9500 R.P.M). 2 grams of sodium alginate were dissolved in 98 grams of water, and 25 grams of the solution were added to the solution of gelatin and dodecyl acetate. The whole mixture was homogenized for 5 minutes (9500 R.P.M). The solution was sprayed through an atomizer (BETE fog nozzle FC7, 1/4 XA, cap AC1201) into 150 ml of 1% CaCl_2 solution. The CaCl_2 solution was contained in a 150 mm diameter vessel, and stirred with a magnetic stirrer in a rate of about 120 R.P.M. The rate of spraying was such that few seconds were required for the 50 g addition to take place. The beads formed (0.01-0.3 mm in diameter) were left in the solution for 5 additional minutes. The beads were then separated by filtration through a sieve, washed in water and stored in water. When dried in room temperature, the beads became hard granules of about 0.005-0.15 mm in diameter. Release rate was measured outdoors over prolonged period of time, and it was found that the formulation yields a slow release of the volatile hydrophobic component. The amounts released were as described in Table 3, and in sample J in Table 1.

EXAMPLE 15

Micron-size particles were prepared as in example 14, but using gelatin Type B 225 Bloom as the protein.

The sprayable formulation (micron size particles in 50 ml of water) was added to 15 L of water and sprayed in a cotton field using a backpack sprayer. Release rate was measured outdoors over prolonged period of time, and it was found that the formulation yields a slow release of the volatile hydrophobic component. The amounts released were as described in Table 3, and in sample K in Table 1.

Reference traps containing pheromone impregnated in cardboard were placed in the middle of the square and in the field, away from the experiment. In a 21 days

period, the reference traps in the field around the experiment trapped much more moths than the trap in the middle of the square as described in Table 4.

EXAMPLE 16

3 grams of gelatin type B 75 Bloom were dissolved in 97 grams of water. 5 grams of Codling moth pheromone and 3.4 grams of water were added to 16.6 grams of the solution, and the mixture was homogenized for 5 minutes (9500 R.P.M). 24 grams of acrylate solution (Joncryl SCX 8089) were dissolved in 6 grams of water, and 25 grams of the solution were added to the solution of gelatin and pheromone. The whole mixture was homogenized for 5 minutes (9500 R.P.M).

The solution was added dropwise through a syringe equipped with a 22G x 1 ½ needle, falling a distance of 60 mm, into 150 ml of 5% CaCl₂ solution. The CaCl₂ solution was contained in a 150 mm diameter vessel, and stirred with a magnetic stirrer in a rate of about 120 R.P.M. The rate of addition was such that 5 minutes were required for the 50g addition to take place. The beads formed (2 mm in diameter) were left in the solution for 5 additional minutes. The beads were then separated by filtration through a sieve, washed in water and stored in water. When air-dried, the beads became hard granules of about 1 mm in diameter.

EXAMPLE 17

Beads were made in the same manner as in example 1, using Codling moth pheromone.

EXAMPLE 18

An emulsion was made in the same manner as in example 16. The emulsion was added to a gellant solution of CaCl₂ 5% using a spraying device as in Example 14, to form micron size particles.

EXAMPLE 19

An emulsion was made in the same manner as in example 16 and added dropwise to 150 ml of glacial acetic acid to form beads of around 2 mm in diameter. The beads were left in the acid for about 5 minutes and then filtered and washed thoroughly with water to remove the acid.

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EXAMPLE 20

An emulsion was made in the same manner as in example 16. The emulsion was added to a glacial acetic acid using a spraying device as in example 14, to form micron size particles. The particles were left in the acid for few minutes and then filtered and washed with water and kept wet in water.

EXAMPLE 21

0.5 g of Tween 80 were added to 5 grams of Codling- moth pheromone and 19.5 grams of water, and the mixture was homogenized for 5 minutes (9500 R.P.M). 2 g of sodium alginate were dissolved in 98 grams of water, and 25 grams of the solution were added to the emulsion of the pheromone and Tween 80. The whole mixture was homogenized for 5 minutes (9500 R.P.M).

The solution was added dropwise through a syringe equipped with a 22G x 1 ½ needle, falling a distance of 60 mm, into 150 ml of 5% CaCl₂ solution. The CaCl₂ solution was contained in a 150 mm diameter vessel, and stirred with a magnetic stirrer in a rate of about 120 R.P.M. The rate of addition was such that 5 minutes were required for the 50g addition to take place. The beads formed (2 mm in diameter) were left in the solution for 5 additional minutes. The beads were then separated by filtration through a sieve, washed in water and stored in water. When air-dried, the beads became hard granules of about 1 mm in diameter.

EXAMPLE 22

An emulsion was made in the same manner as in example 21. The emulsion was added to a gellant solution of CaCl₂ 1% using a spraying device as in example 14, to form micron size particles.

EXAMPLE 23

0.5 g of Tween 80 were added to 5 grams of Codling- moth pheromone and 19.5 grams of water, and the mixture was homogenized for 5 minutes (9500 R.P.M). 24 grams of acrylate solution (Joncryl SCX 8089) were dissolved in 6 grams of water, and 25 grams of the solution were added to the solution of Tween 80 and pheromone. The whole mixture was homogenized for 5 minutes (9500 R.P.M). The solution was added dropwise through a syringe equipped with a 22G x 1 ½ needle, falling a distance of 60 mm, into 150 ml of 5% CaCl₂ solution. The CaCl₂ solution was contained in a 150 mm diameter vessel, and stirred with a magnetic stirrer in a rate of about 120 R.P.M. The rate of addition was such that 5 minutes

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were required for the 50g addition to take place. The beads formed (2 mm in diameter) were left in the solution for 5 additional minutes. The beads were then separated by filtration through a sieve, washed in water and stored in water. When air-dried, the beads became hard granules of about 1 mm in diameter.

EXAMPLE 24

An emulsion was made in the same manner as in example 23. The emulsion was added to a gellant solution of CaCl_2 5% using a spraying device as in example 14, to form micron size particles.

EXAMPLE 25

An emulsion was made in the same manner as in example 23 and added dropwise to 150 ml of glacial acetic acid to form beads of around 2 mm in diameter. The beads were left in the acid for about 5 minutes and then filtered and washed thoroughly with water to remove the acid.

EXAMPLE 26

An emulsion was made in the same manner as in example 23. The emulsion was added to a glacial acetic acid using a spraying device as in example 14, to form micron size particles. The particles were left in the acid for few minutes and then filtered and washed with water and kept wet in water.

Using the beads and micron size particles made by the examples above, the amount of volatile material released to the atmosphere was measured resulting in the amounts outlined in Table 1.

TABLE 1:

Sample	Example	Wet Bead diameter (mm)	Dry bead diameter (mm)	Wet bead Weight (mg)	Dry bead Weight (mg)	weight of active ingredient released (% of total)
A	1	1.5 - 2	1 - 1.5	4 - 5	1 - 2	32 (after 63 days)
B	2	1.5 - 2	1 - 1.5	4 - 5	1 - 2	45 (after 37 days)
C	3	1.5 - 2	1 - 1.5	4 - 5	1 - 2	35 (after 37 days)
D	4	1.5 - 2	1 - 1.5	4 - 5	1 - 2	10 (after 52 days)
E	5	1.5 - 2	1 - 1.5	4 - 5	1 - 2	80 (after 52 days)
F	6	1.5 - 2	1 - 1.5	4 - 5	1 - 2	75 (after 63 days)
G	9	1 - 1.5	1	4 - 5	1 - 2	50 (after 42 days)
H	10	1.5 - 2	1 - 1.5	4 - 5	1 - 2	40 (after 90 days)
I	11	2 - 3	0.5 - 1	5	0.5 - 1	85 (after 21 days)
J	14	0.005-0.1	—	—	—	90 (after 22 days)
K	15	0.005-0.1	—	—	—	65 (after 37 days)

TABLE 2:

	Average number of moths per trap per day					
	After 5 days	After 7 days	After 13 days	After 24 days	After 37 days	After 43 days
Experiment	0	3	1	2	0	3
Control	12	32 *	9	42 *	40	30

* The field was sprayed against PBW one day after the count.

TABLE 3:

Number of days	0	5	10	15	22	35
Percent released 75 Bloom	0	25	70	80	90	95
Percent released 225 Bloom	0	18	35	40	50	70

TABLE 4:

Average number of moths per trap per day			
	After 5 days	After 12 days	After 20 days
Experiment	0	0	1
Control	7.5	16	25

It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrative examples and that the present invention may be embodied in other specific forms without departing from the essential attributes thereof, and it is therefore desired that the present embodiments and examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

WHAT IS CLAIMED IS:

1. A sustained release, polymer-based, water insoluble bead, comprising a polymeric matrix containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.
2. A sustained release, polymer-based, water insoluble bead, according to claim 1 wherein said polymeric matrix comprises at least one polymer selected from the group consisting of a protein, a polysaccharide and a synthetic polymer.
3. A sustained release, polymer-based, water insoluble bead, according to claim 2 wherein said protein is selected from the group consisting of gelatin, albumin, casein and Lactoglobulin.
4. A sustained release, polymer-based, water insoluble bead, according to claim 2, wherein said polysaccharide is selected from the group consisting of sodium alginate, chitin, carraggenan, guar gum, locus bean gum, chitosan, pectin carboxy methyl cellulose.
5. A sustained release, polymer-based, water insoluble bead, according to claim 1, wherein said surface active molecule is selected from the group consisting of a protein, a monomeric surfactant and a polymeric surfactant.
6. A sustained release, polymer-based, water insoluble bead, according to claim 1, wherein said surface active molecule is selected from the group consisting of ethoxylated sorbitan ester, alkyl ether, a block copolymer and gelatin.
7. A sustained release, polymer-based, water insoluble bead, according to claim 1, wherein said bead is of a size between 0.5 micron and 1 mm.
8. A sustained release, polymer-based, water insoluble bead, according to claim 1, wherein said bead is of a size between 5 and 80 microns.

9. A sustained-release polysaccharide-protein water insoluble bead, according to claim 1, comprising an emulsion of at least one protein and at least one volatile hydrophobic component contained therein, wherein said volatile component is released from said water insoluble bead in atmospheric air.
10. A sustained-release polymer-based, water insoluble bead, according to claim 1, wherein said volatile component is a bioactive material.
11. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is pheromone.
12. A sustained-release polymer-based bead according to claim 11, wherein said pheromone is selected from the group consisting of grandlure, muscalure, gossyplure and disparlure.
13. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is an essential oil.
14. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is a pesticide.
15. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is an attractant.
16. A sustained-release polymer-based bead according to claim 15, wherein said attractant is selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.
17. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is an attractant inhibitor.

18. A sustained-release polymer-based bead according to claim 17, wherein said attractant inhibitor is selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.
19. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is present in an amount of up to 50% wt./wt.
20. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is present in an amount of up to 20% wt./wt.
21. A sustained-release polymer-based bead according to claim 1, wherein said protein is a gelatin.
22. A sustained-release polymer-based bead according to claim 21, wherein said gelatin is a type B gelatin.
23. A sustained-release polymer-based bead according to claim 1, wherein said volatile component is Eugenol.
24. A sustained-release polymer-based bead according to claim 1, further comprising tannic acid for effecting a slower release rate.
25. A process for preparing sustained-release polymer-based water insoluble beads for release of a volatile hydrophobic component therefrom in atmospheric air, comprising:
- a) preparing an oil/water emulsion by homogenizing a volatile hydrophobic component in water, using at least one surface active molecule;
 - b) mixing said emulsion with at least one water-soluble polymer and optionally rehomenizing the mixture; and
 - c) adding the emulsion prepared in step (b) in a dropwise manner into a gellant solution to form said water insoluble beads.

26. A process according to claim 25, further comprising the step of chemically cross-linking polymers present in said composition.
27. A process according to claim 25, further comprising the step of drying said beads.
28. A process according to claim 25, wherein said gellant solution is selected from the group consisting of an electrolyte solution, a multivalent ion solution, a lower pH solution and a high pH solution.
29. A process according to claim 25, wherein said volatile component is a bioactive material.
30. A process according to claim 25, wherein said volatile component is pheromone.
31. A process according to claim 30, wherein said pheromone is selected from the group consisting of grandlure, muscalure, gossyplure and disparlure.
32. A process according to claim 25, wherein said volatile component is an essential oil.
33. A process according to claim 25, wherein said volatile component is a pesticide.
34. A process according to claim 25, wherein said volatile component is an attractant.
35. A process according to claim 34, wherein said attractant is selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.
36. A process according to claim 25, wherein said volatile component is an attractant inhibitor.

37. A process according to claim 36, wherein said attractant inhibitor is selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.
38. A process according to claim 25, wherein said volatile component is present in an amount of up to 50% wt./wt.
39. A process according to claim 25, wherein said volatile component is present in an amount of up to 20% wt./wt.
40. A process according to claim 25, wherein said surface active molecule is a gelatin.
41. A process according to claim 40, wherein said gelatin is a type B gelatin.
42. A process according to claim 25, wherein said gellant is an aqueous metal salt solution.
43. A process according to claim 42, wherein said aqueous metal salt solution comprises a divalent, trivalent or quatra-valent metal salt.
44. A process according to claim 42, wherein said metal salt solution comprises chlorides and acetates of calcium, barium, copper and tin.
45. A process according to claim 25, wherein the emulsion of step (b) is sprayed into said gellant to form micron-sized beads.
46. A process according to claim 25, wherein said polymer is a polysaccharide.
47. A process according to claim 46, wherein said polysaccharide is alginate.

- 48 A process according to claim 47, wherein said alginate is a water-soluble salt of alginic acid.
- 49 A process according to claim 47, wherein said alginate is a water-soluble salt of organic bases.
- 50 A process according to claim 47, wherein said alginate is selected from the group consisting of sodium, potassium, magnesium, ammonium alginate and amines.
- 51 A process according to claim 47, wherein said alginate is present in an amount of about between 0.1 and 5% wt./wt.
- 52 A process according to claim 47, wherein said alginate is present in an amount of about between 1 and 1.5% wt./wt.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 99/00660

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01N25/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01N A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 198334 Derwent Publications Ltd., London, GB; Class A97, AN 1983-744808 XP002136272 & JP 58 121212 A (NITTO ELECTRIC IND CO), 19 July 1983 (1983-07-19) abstract ---	1,2,5, 10-20
X	GB 2 129 302 A (CHEMICAL DISCOVERIES SA) 16 May 1984 (1984-05-16) whole document ---	1,2,5-7, 10-20
A	US 4 401 456 A (CONNICK JR WILLIAM J) 30 August 1983 (1983-08-30) cited in the application --- -/--	

☒ Further documents are listed in the continuation of box C.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MEINKE L J ET AL: "PHEROMONE DELIVERY SYSTEM: WESTERN CORN ROOTWORM (COLEOPTERA: CHRYSOMELIDAE) PHEROMONE ENCAPSULATION IN A STARCH BORATE MATRIX"</p> <p>JOURNAL OF ECONOMIC ENTOMOLOGY, US, ENTOMOLOGICAL SOCIETY OF AMERICA. COLLEGE PARK, MARYLAND, vol. 82, no. 6, 1 December 1989 (1989-12-01), pages 1830-1835, XP000086080 ISSN: 0022-0493</p> <p style="text-align: center;">---</p>	
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A	<p>EP 0 617 051 A (ALLIED COLLOIDS LTD) 28 September 1994 (1994-09-28)</p> <p style="text-align: center;">-----</p>	

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		NO 891651 A	20-06-1989

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/IL99/00660 (22) International Filing Date: 3 December 1999 (03.12.99) (30) Priority Data: 127396 3 December 1998 (03.12.98) IL (71) Applicants (for all designated States except US): BEN GURION UNIVERSITY OF THE NEGEV RESEARCH AND DEVELOPMENT AUTHORITY [IL/IL]; P.O. Box 653, 84105 Beer Sheva (IL). YISSUM RESEARCH DEVELOPMENT COMPANY [IL/IL]; The Hebrew University of Jerusalem, P.O. Box 4279, 91042 Jerusalem (IL). (72) Inventors; and (75) Inventors/Applicants (for US only): SHANI, Arnon [IL/IL]; Ha'oren Street 18, 84965 Omer (IL). MAGDASSI, Shlomo [IL/IL]; Hanerd Street 36, 96626 Jerusalem (IL). YOSHA, Ido [IL/IL]; Kibbutz Kfar-Aza, 85142 Mobile Post Hanegev (IL). (74) Agent: WOLFF, BREGMAN AND GOLLER; P.O. Box 1352, 91013 Jerusalem (IL).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>With amended claims.</i> Date of publication of the amended claims: 8 September 2000 (08.09.00)
(54) Title: SUSTAINED RELEASE POLYMER-BASED WATER INSOLUBLE BEADS (57) Abstract The invention provides a sustained release, polymer-based, water insoluble bead, comprising a polymeric matrix containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.		

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AMENDED CLAIMS

[received by the International Bureau on 13 June 2000 (13.06.00);
original claims 1-52 replaced by amended claims 1-52 (5 pages)]

1. A sustained release dispersion of water insoluble beads, each bead comprising a polymeric matrix containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.
2. A sustained release dispersion of water insoluble beads according to claim 1 wherein said polymeric matrix comprises at least one polymer selected from the group consisting of a protein, a polysaccharide and a synthetic polymer.
3. A sustained release dispersion of water insoluble beads according to claim 2, wherein said protein is selected from the group consisting of gelatin, albumin, casein and Lactoglobulin.
4. A sustained release dispersion of water insoluble beads according to claim 2, wherein said polysaccharide is selected from the group consisting of sodium alginate, carraggenan, guar gum, locus bean gum, chitosan, pectin carboxy methyl cellulose.
5. A sustained release dispersion of water insoluble beads according to claim 1, wherein said surface active molecule is selected from the group consisting of a protein, a monomeric surfactant and a polymeric surfactant.
6. A sustained release dispersion of water insoluble beads according to claim 1, wherein said surface active molecule is selected from the group consisting of ethoxylated sorbitan ester, alkyl ether, a block copolymer and gelatin.
7. A sustained release dispersion of water insoluble beads according to claim 1, wherein each of said beads is of a size between 0.5 micron and 1 mm.

8. A sustained release dispersion of water insoluble beads according to claim 1, wherein each of said beads is of a size between 5 and 80 microns.
9. A sustained-release polysaccharide-protein water insoluble beads according to claim 1, comprising an emulsion of at least one protein and at least one volatile hydrophobic component contained therein, wherein said volatile component is released from said water insoluble bead in atmospheric air.
10. A sustained-release dispersion of water insoluble beads according to claim 1, wherein said volatile component is a bioactive material.
11. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is a pheromone.
12. A sustained-release dispersion of bead according to claim 11, wherein said pheromone is selected from the group consisting of grandlure, muscalure, gosiplure and disparlure.
13. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is an essential oil.
14. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is a pesticide.
15. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is an attractant.
16. A sustained-release dispersion of bead according to claim 15, wherein said attractant is selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.
17. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is an attractant inhibitor.
18. A sustained-release dispersion of bead according to claim 17, wherein said attractant inhibitor is selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.

19. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is present in an amount of up to 50% wt./wt.
20. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is present in an amount of up to 20% wt./wt.
21. A sustained-release dispersion of bead according to claim 1, wherein said protein is a gelatin.
22. A sustained-release dispersion of bead according to claim 21, wherein said gelatin is a type B gelatin.
23. A sustained-release dispersion of bead according to claim 1, wherein said volatile component is Eugenol.
24. A sustained-release dispersion of bead according to claim 1, further comprising tannic acid for effecting a slower release rate.
25. A process for preparing a sustained-release dispersion of water insoluble beads for release of a volatile hydrophobic component therefrom in atmospheric air, comprising:
 - a) preparing an oil/water emulsion by homogenizing a volatile hydrophobic component in water, using at least one surface active molecule;
 - b) mixing said emulsion with at least one water-soluble polymer and optionally rehomenizing the mixture; and
 - c) adding the emulsion prepared in step (b) in a dropwise manner into a gellant solution to form said water insoluble beads.
26. A process according to claim 25, further comprising the step of chemically cross-linking polymers present in said composition.
27. A process according to claim 25, further comprising the step of drying said beads.
28. A process according to claim 25, wherein said gellant solution is selected from the group consisting of an electrolyte solution, a multivalent ion solution, a lower pH solution and a high pH solution.

29. A process according to claim 25, wherein said volatile component is a bioactive material.
30. A process according to claim 25, wherein said volatile component is A pheromone.
31. A process according to claim 30, wherein said pheromone is selected from the group consisting of grandlure, muscalure, gosiplure and disparlure.
32. A process according to claim 25, wherein said volatile component is an essential oil.
33. A process according to claim 25, wherein said volatile component is a pesticide.
34. A process according to claim 25, wherein said volatile component is an attractant.
35. A process according to claim 34, wherein said attractant is selected from the group consisting of eugenol, benzyl alcohol, leaf alcohols, aldehydes and acetates.
36. A process according to claim 25, wherein said volatile component is an attractant inhibitor.
37. A process according to claim 36, wherein said attractant inhibitor is selected from the group consisting of (Z)-9-tetradecenyl formate and (E,E)-10,12-hexadecadienol.
38. A process according to claim 25, wherein said volatile component is present in an amount of up to 50% wt./wt.
39. A process according to claim 25, wherein said volatile component is present in an amount of up to 20% wt./wt.
40. A process according to claim 25, wherein said surface active molecule is a gelatin.
41. A process according to claim 40, wherein said gelatin is a type B gelatin.
42. A process according to claim 25, wherein said gellant is an aqueous metal salt solution.

43. A process according to claim 42, wherein said aqueous metal salt solution comprises a divalent or trivalent metal salt.
44. A process according to claim 42, wherein said metal salt solution comprises chlorides and acetates of calcium, barium and copper.
45. A process according to claim 25, wherein the emulsion of step (b) is sprayed into said gellant to form micron-sized beads.
46. A process according to claim 25, wherein said polymer is a polysaccharide.
47. A process according to claim 46, wherein said polysaccharide is alginate.
48. A process according to claim 47, wherein said alginate is a water-soluble salt of alginic acid.
49. A process according to claim 47, wherein said alginate is a water-soluble salt of organic bases.
50. A process according to claim 47, wherein said alginate is selected from the group consisting of sodium, potassium, magnesium, ammonium alginate and amines.
51. A process according to claim 47, wherein said alginate is present in an amount of about between 0.1 and 5% wt./wt.
52. A process according to claim 47, wherein said alginate is present in an amount of about between 1 and 1.5% wt./wt.

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<p>(21) International Application Number: PCT/IL99/00660</p> <p>(22) International Filing Date: 3 December 1999 (03.12.99)</p> <p>(30) Priority Data: 127396 3 December 1998 (03.12.98) IL</p> <p>(71) Applicants (for all designated States except US): BEN GU-RION UNIVERSITY OF THE NEGEV RESEARCH AND DEVELOPMENT AUTHORITY [IL/IL]; P.O. Box 653, 84105 Beer Sheva (IL). YISSUM RESEARCH DEVELOPMENT COMPANY [IL/IL]; The Hebrew University of Jerusalem, P.O. Box 4279, 91042 Jerusalem (IL).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): SHANI, Amon [IL/IL]; Ha'oren Street 18, 84965 Omer (IL). MAGDASSI, Shlomo [IL/IL]; Hanerd Street 36, 96626 Jerusalem (IL). YOSHA, Ido [IL/IL]; Kibbutz Kfar-Aza, 85142 Mobile Post Hanegev (IL).</p> <p>(74) Agent: WOLFF, BREGMAN AND GOLLER; P.O. Box 1352, 91013 Jerusalem (IL).</p>		<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: SUSTAINED RELEASE POLYMER-BASED WATER INSOLUBLE BEADS</p>		
<p>(57) Abstract</p> <p>The invention provides a sustained release, polymer-based, water insoluble bead, comprising a polymeric matrix containing a plurality of emulsion droplets, said droplets being formed from at least one surface active molecule, at least one volatile hydrophobic component and water, wherein said volatile component is released from said water insoluble bead in atmospheric air.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01N A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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